

Malignant melanoma over a fifty-year period: a histological evaluation

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SUMMARY

The incidence of primary cutaneous malignant melanoma is increasing in the developed countries. Cutaneous malignant melanomas diagnosed in our Department over a period of fifty years from 1930 to 1980 were examined to see if there was any change in their histological features. In 1930 and 1955, over 90% of malignant melanomas presented as tumours infiltrating deep into the subepithelial tissue. By 1980, 55% of tumours presented with deeply infiltrating lesions and only 20% occurred at a stage where adequate local excision could provide hope of a cure. There is thus a need for greater awareness among the medical profession and the public if we hope to be able to treat malignant melanomas at an early stage.

INTRODUCTION

Malignant melanoma is a malignant tumour arising from the melanocytes in the skin. It is the most common fatal illness seen by the dermatologist, and accounts for 1 % of all cancer deaths.¹ The incidence of malignant melanoma of the skin is increasing in both sexes in developed countries, notably in fair-skinned people. It is thought that this increased incidence is related to an increase of intense and intermittent exposure to the sun. Associated with the increased incidence of malignant melanoma there have been reports of better overall survival, especially in areas like Queensland, where greater medical and public awareness ensure that the lesions are seen at an earlier stage of their development.^{2, 3} This study is part of an ongoing multinational sixteen-centre project, funded by the International Agency for Research on Cancer of the World Health Organisation, to find out if there is a possibility that part of the rise in incidence is due to a change in the histological criteria used in the diagnosis of malignant melanoma.

The aim of the present study was to look at malignant melanoma presenting to our Department over a fifty-year period to see if there was any change in the histological features of the tumours and if the lesions present today at an earlier stage than they did in the past.

METHODS

Twenty lesions diagnosed as malignant melanoma were examined from the files of the Department of Pathology, Royal Victoria Hospital, Belfast, for each of three periods in 1930, 1955 and 1980. The cases were taken from the files in chronological order until 20 cases of primary cutaneous malignant melanoma were reached. In 1930 and 1955, where 20 cases were not available during the

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year, cases were taken from further years (i.e. 1931, 1956, etc.) until 20 cases were obtained. Secondary malignant melanomas occurring in the skin and non-cutaneous primary malignant melanoma were excluded from the study. The original reports were examined to obtain information about the age and sex of the patient and the site of biopsy. The original slides for the 1980 cases were available for review in the laboratory. For the periods 1930 and 1955 the original blocks were available and sections were recut. It was not known whether the blocks from the 1930 and 1955 cases had been taken from the deepest part of the tumour. If the blocks in the earlier years were not taken from the deepest part of the tumour, it can be assumed that both the Clark level and Breslow's thickness were greater than the values we obtained. The blocks in the 1980 cases were taken from the deepest part of the tumour.

In each case the following were noted:-

(a) sex of patient; (b) age of patient; (c) site of biopsy.

Microscopically the following features were recorded:-

(d) histogenetic type; (e) cross-sectional profile; (f) ulceration; (g) inflammatory infiltrate; (h) degree of pigmentation; (i) cell type; (j) evidence of regression; (k) vascular invasion; (l) evidence of pre-existing lesion; (m) elastosis; (n) Clark level; (o) tumour diameter; (p) tumour depth (Breslow's thickness); (q) number of mitoses/H.P.F. (X 40); (r) mitotic rate (mitoses/sq. mm); (s) prognostic index (tumour depth \times mitotic rate) ($p \times r$).

RESULTS

M:F Ratios

In each of the three time periods studied, the number of females was greater than the number of males and this is in keeping with the results in the literature.^{4, 5, 6} There was a greater female to male ratio in the year 1980 of 2.3:1, compared with 1930 and 1955 when the ratio was 1.5:1.

Age

Malignant melanoma presented with a greater incidence from the fifth decade onwards in all three time periods. In the overall time studied there does not appear to be any change in the age group affected in the disease.

Site

The head and neck are the most common sites for the tumour to arise. The trunk, an area of relatively low sun exposure in this country, has a low incidence of tumour and there has been no change in the incidence over the period of the present study. (Table I).

TABLE I
Site of biopsy

	1930	1955	1980
Head and neck	6 (30%)	4 (20%)	8 (40%)
Trunk	2 (10%)	2 (10%)	3 (15%)
Upper limb	6 (30%)	5 (25%)	0 (0%)
Lower limb	3 (15%)	0 (0%)	7 (35%)
Site unknown	3 (15%)	9 (45%)	2 (10%)
	20 cases	20 cases	20 cases

Morphology

Almost half the tumours in the 1930 and 1955 groups and a quarter of the 1980 cases could not be classified by histogenic type.⁷ The most common type of tumour was the superficial spreading malignant melanoma which accounted for 50% of the 1980 tumours and 40% of the 1930 tumours. Lentigo malignant melanoma only occurred in the 1955 and 1980 tumours, accounting for 5% and 15% respectively. (Table II).

TABLE II
Histogenic type

	1930	1955	1980
Lentigo malignant melanoma	0 (0%)	1 (5%)	3 (15%)
Superficial spreading malignant melanoma	8 (40%)	7 (35%)	10 (50%)
Nodular malignant melanoma	2 (10%)	3 (15%)	2 (10%)
Unclassifiable	10 (50%)	9 (45%)	5 (25%)
	20 cases	20 cases	20 cases

In the study, 45% of the 1930 tumours and 55% of the 1955 and 1980 tumours were predunculated. On average, over the time of the study, 50% of the lesions were ulcerated, had a light to moderate inflammatory cell infiltrate, and a mild to moderate degree of pigment, and these factors did not change over the period examined. The cell type predominant in the lesion did not show any significant change over the study period. Spindle cells were predominant in 55% (1930), 40% (1955) and 60% (1980) respectively. In none of the 60 malignant melanomas examined was there evidence of regression of the tumour.

Vascular invasion

Vascular invasion was noted in one case from both 1930 and 1980 and in two of the 1955 cases. When present, vascular invasion indicates a high risk of metastatic spread.⁸

Association with benign lesions

In the 1930 tumours, three of the malignant melanomas were associated with benign lesions: a compound naevus and two intradermal naevi. There was one case in the 1955 series where a compound naevus was associated with the malignant melanoma. Five of the 20 malignant melanomas of the 1980 cases were associated with the following lesions: lentigo, compound naevus, two intradermal naevi and a neurofibroma.

Elastosis

Elastosis due to sun damage was noted in 30% of the 1980 lesions and in 10% and 5% of the 1955 and 1930 lesions. All the cases of elastosis occurred in malignant melanomas arising in the head and neck.

Clark's levels

In 1930 no cases of Clark^{7,9} level I (tumour confined to the epidermis) were recorded, and only 5% of cases in 1955 and 1980 had a Clark level I. In 1930, 80% of cases presented with Clark level IV and V (tumour involving the reticular

dermis and subcutaneous fat respectively), compared with 75% of cases in 1955, and 50% of cases in 1980. In 1980, 5% of these cases were at a Clark level V. (Table III).

TABLE III
Clark level

<i>Level</i>	<i>1930</i>	<i>1955</i>	<i>1980</i>
I	0 (0%)	1 (5%)	1 (5%)
II	2 (10%)	2 (10%)	2 (10%)
III	2 (10%)	2 (10%)	7 (35%)
IV	9 (45%)	12 (60%)	9 (45%)
V	7 (35%)	3 (15%)	1 (5%)
	20 cases	20 cases	20 cases

Thickness and diameter

The tumour thickness of each lesion was measured using the method described by Breslow.^{10, 11} In 1930, 95% of the tumours and, in 1955, 90% of the tumours had a Breslow thickness of more than 1.5mm. In 1980, 55% of cases presented with a Breslow thickness of greater than 1.5mm while 20% of cases had a Breslow thickness of less than 0.76mm and 25% were in the intermediate range of 0.76–1.5mm. (Table IV). In 1930, 65% of the tumours had a diameter greater than 11mm. In 1955, 45% of tumours had a diameter of more than 11mm and in 1980, 20% had a tumour with a diameter greater than 11mm.

TABLE IV
Breslow's thickness

	<i>1930</i>	<i>1955</i>	<i>1980</i>
< 0.76mm	1 (5%)	1 (5%)	4 (20%)
0.76–1.5mm	0 (0%)	1 (5%)	5 (25%)
1.5–3mm	7 (35%)	8 (40%)	7 (35%)
> 3mm	12 (60%)	10 (50%)	4 (20%)
	20 cases	20 cases	20 cases

Mitoses

The percentage of cases with fewer than one mitosis/5 high power fields was 20% in 1930, 55% in 1955, and 50% in 1980. There were 25% of 1930 cases, 20% of 1955 cases and 15% of 1980 cases with more than five mitoses/5 high power fields. The mitotic rate (number of mitoses per square millimetre) shows a slight fall over the period of the study.¹¹ In 1930, 20% of cases had a mitotic rate of nil compared with 40% in 1955 and 50% in 1980. (Table V).

Prognostic index

The prognostic index¹² (the product of tumour thickness and mitotic index) was less than 13 in 40% of cases in 1930, in 40% of cases in 1955 and in 65% of cases in 1980.

TABLE V
Mitotic rate

	1930	1955	1980
0	4 (20%)	8 (40%)	10 (50%)
1 – 5	7 (35%)	3 (15%)	4 (20%)
6 – 10	4 (20%)	5 (25%)	4 (20%)
11 – 20	4 (20%)	2 (10%)	1 (5%)
21 – 30	0 (0%)	2 (10%)	0 (0%)
31 – 40	1 (5%)	0 (0%)	1 (5%)
	20 cases	20 cases	20 cases

DISCUSSION

In both the 1930 and 1955 samples, cases had to be taken from more than one year to reach the required sample number in our study. This may be due to the increasing incidence of malignant melanoma, but in the earlier years malignant melanoma may have been removed and not submitted for histological examination. Over the fifty-year period of the study there has been little change in the sex, age and site on the body of the tumour of patients presenting with malignant melanoma. The predominant cell type showed little variation over the fifty-year period as did the presence or absence of ulceration.

Superficial spreading malignant melanoma was the most common histogenic type of tumour over the three periods examined. Lentigo malignant melanoma occurred only in the 1955 and 1980 samples and the incidence is higher in the latter. Lentigo malignant melanoma is a slow-growing tumour and perhaps this is why patients and doctors in 1930 appear to have ignored this lesion or at least tended not to remove it. Patients in earlier years with lentigo malignant melanoma may have presented at such a late stage in their tumour's development that accurate histogenic classification was not possible. Pedunculated tumours were most common in all the periods studied and did not show any significant variation over the fifty-year period. Vascular invasion showed no significant change over the period of the study. The association with a pre-existing lesion was more common in the 1980 cases than in the earlier years but the tumours arising in the earlier years were larger and may have destroyed any pre-existing benign lesion.

Solar damage to the skin was more commonly noted in 1980 cases than in earlier years, although the increasing number of lesions arising in the head and neck, especially the lentigo malignant melanoma type of tumour, could not have accounted solely for this. The occurrence of malignant melanoma with solar damage is increasing through the decades as seen in this series.

The number of patients in the series presenting with tumour confined to the epidermis (Clark's level I) is depressingly low: only 5% in both 1955 and 1980. There has been no change in the latter twenty-five years, when there has been an increasing awareness of the improved prognosis with early treatment of the lesion. More cases in 1980 than in earlier years were presenting with a Clark's level II or III, but it is depressing still to find 50% of cases in 1980 occurring with Clark's level IV or V, as compared with 80% in 1930 and 75% in 1955. Breslow's index of the thickness of the tumour showed a similar pattern. In 1930 and 1955

over 90% of tumours had a thickness of 1.5mm which is associated with a poor prognosis. In 1980, 55% of cases are still presenting with a thickness of greater than 1.5mm. Only 20% of cases in 1980 had a tumour thickness of less than 0.76mm, which is associated with a good prognosis.

Over the years of the study there was a steady decrease in the tumour diameter of the lesions, indicating that the tumours were presenting at a smaller size. There was a steady decrease from 25% in 1930 to 15% in 1980 of tumours with more than 5 mitoses/5 high power fields, and an increase in the number of cases with a low mitotic count. A prognostic index of less than 13 showed an increase in the number of cases from 1955 to 1980.

Gordon and Lowry found that over 75% of malignant melanoma present in Northern Ireland over the five-year period of 1974-1978 had a tumour thickness of greater than 1.5mm.⁶ Our results support their finding that the majority of patients in Northern Ireland still present with malignant melanoma at a late stage with poor histological criteria and at a high risk of metastatic spread. The most likely reason for the large number of malignant melanoma presenting with poor histological criteria is lack of awareness, by both the public and the medical profession, of the importance of early diagnosis and treatment of these lesions. If patients with malignant melanoma are to present at a stage where local excision offers adequate cure and treatment, there is need for increased education of both the public and the medical profession.

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